



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 122956

TO: Kevin Weddington
Location: REM-4B87/4C70
Art Unit: 1614
Wednesday, June 02, 2004

Case Serial Number: 10/031708

From: Peggy Ruppel
Location: Biotech-Chem Library
REMSSEN 1B65
Phone: 571-272-2557

Peggy.Ruppel@uspto.gov

Search Notes

Examiner Weddington,

I've kept a complete record of the structures that I retrieved for this search, so that you can view all of them if you would like.

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STIC SEARCH RESULTS FEEDBACK FORM

Biotech Chem Library

Questions about the scope or the results of the search? Contact the searcher or contact:

Mary Hale, Information Branch Supervisor
308-4258, CM1-1E01

Voluntary Results Feedback Form

➤ I am an examiner in Workgroup: Example: 1610

➤ Relevant prior art found, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art not found:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech Chem Library CM1 - Ctr. Desk



=> b reg

FILE 'REGISTRY' ENTERED AT 11:48:35 ON 02 JUN 2004
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 1 JUN 2004 HIGHEST RN 688308-86-3
DICTIONARY FILE UPDATES: 1 JUN 2004 HIGHEST RN 688308-86-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

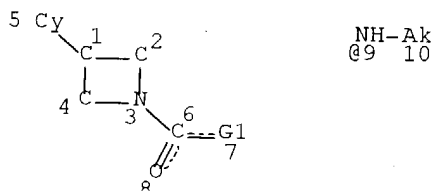
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d que l35

L2 STR



VAR G1=NH2/9

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

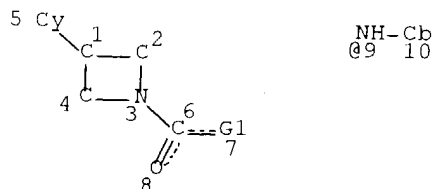
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L4 98 SEA FILE=REGISTRY SSS FUL L2

L32 STR



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DEFAULT ECLEVEL IS LIMITED

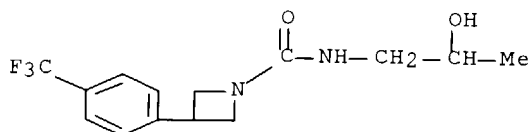
GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE
L34 33 SEA FILE=REGISTRY SSS FUL L32
L35 114 SEA FILE=REGISTRY ABB=ON PLU=ON L4 OR L34

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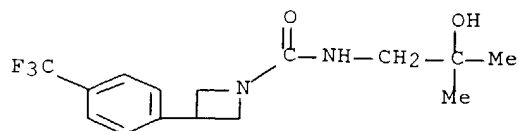
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RN 323204-87-1 REGISTRY
CN 1-Azetidinecarboxamide, N-(2-hydroxypropyl)-3-[4-(trifluoromethyl)phenyl]-
(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C14 H17 F3 N2 O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA Cplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES
(Uses)



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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

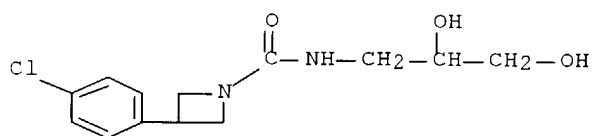
L35 ANSWER 10 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231954-61-3 REGISTRY
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FS 3D CONCORD
MF C15 H19 F3 N2 O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA Cplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC
(Process); PRP (Properties); USES (Uses)



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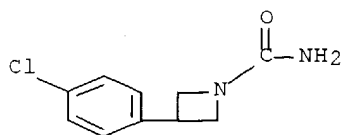
L35 ANSWER 15 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231954-56-6 REGISTRY
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(CA INDEX NAME)
FS 3D CONCORD
MF C13 H17 Cl N2 O3
SR CA
LC STN Files: CA, CAPLUS
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC
(Process); PRP (Properties); USES (Uses)



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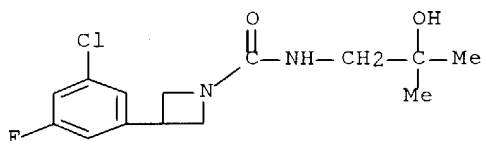
L35 ANSWER 20 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231954-51-1 REGISTRY
CN 1-Azetidinecarboxamide, 3-(4-chlorophenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C10 H11 Cl N2 O
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LC STN Files: CA, CAPLUS
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC
(Process); PRP (Properties); USES (Uses)



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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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RN 231954-46-4 REGISTRY
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FS 3D CONCORD
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SR CA
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RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

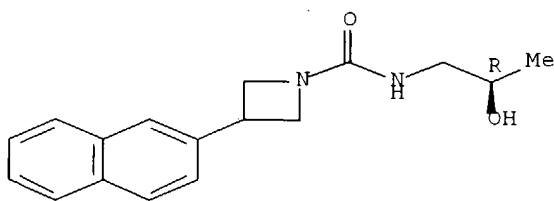


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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 30 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231954-41-9 REGISTRY
CN 1-Azetidinecarboxamide, N-[(2R)-2-hydroxypropyl]-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C17 H20 N2 O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.

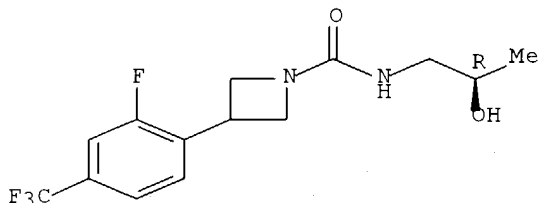


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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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RN 231954-36-2 REGISTRY
CN 1-Azetidinecarboxamide, 3-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(2R)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C14 H16 F4 N2 O2
SR CA
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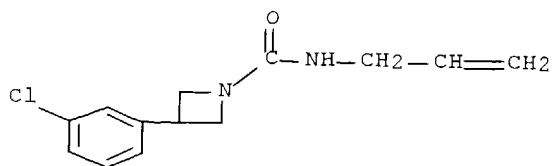
Absolute stereochemistry.



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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 40 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231954-29-3 REGISTRY
CN 1-Azetidinecarboxamide, 3-(3-chlorophenyl)-N-2-propenyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C13 H15 Cl N2 O
SR CA
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RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

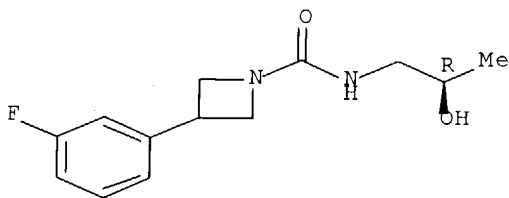


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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 45 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231954-20-4 REGISTRY
CN 1-Azetidinecarboxamide, 3-(3-fluorophenyl)-N-[(2R)-2-hydroxypropyl]- (9CI)
(CA INDEX NAME)
FS STEREOSEARCH
MF C13 H17 F N2 O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC
(Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.

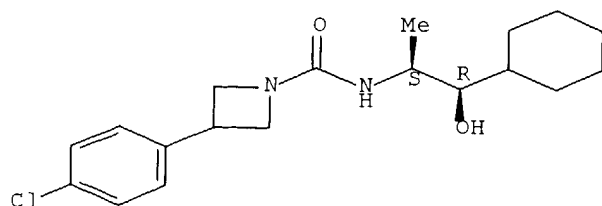


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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 50 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231954-10-2 REGISTRY
CN 1-Azetidinecarboxamide, 3-(4-chlorophenyl)-N-[(1R,2S)-2-cyclohexyl-2-hydroxy-1-methylethyl]-, rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
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LC STN Files: CA, CAPLUS
DT.CA Caplus document type: Patent
RL.P Roles from patents: PROC (Process); PRP (Properties)

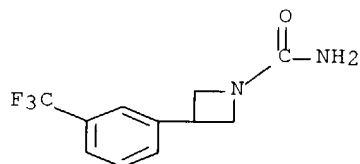
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 55 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231953-99-4 REGISTRY
CN 1-Azetidinecarboxamide, 3-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C11 H11 F3 N2 O
SR CA
LC STN Files: CA, CAPLUS
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)



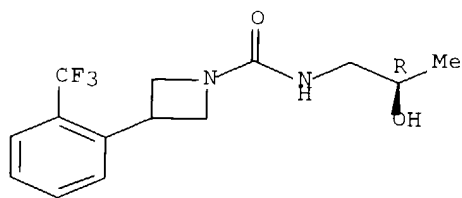
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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 60 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231953-91-6 REGISTRY
CN 1-Azetidinecarboxamide, N-[(2R)-2-hydroxypropyl]-3-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C14 H17 F3 N2 O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.

Searched by P. Ruppel

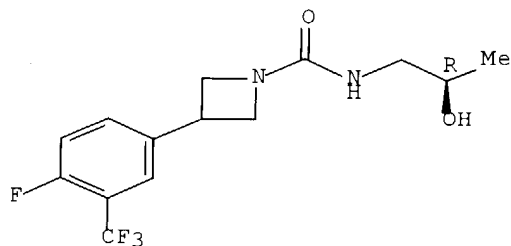


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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 65 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231953-86-9 REGISTRY
CN 1-Azetidinecarboxamide, 3-[4-fluoro-3-(trifluoromethyl)phenyl]-N-[(2R)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C14 H16 F4 N2 O2
SR CA
LC STN Files: CA, CAPLUS
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RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.

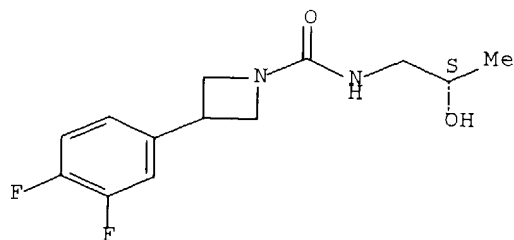


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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 70 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231953-81-4 REGISTRY
CN 1-Azetidinecarboxamide, 3-(3,4-difluorophenyl)-N-[(2S)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C13 H16 F2 N2 O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 75 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN

RN 231953-76-7 REGISTRY

CN 1-Azetidinecarboxamide, N-[(2R)-2-hydroxypropyl]-3-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN (R)-3-(3-Trifluoromethylphenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

FS STEREOSEARCH

MF C14 H17 F3 N2 O2

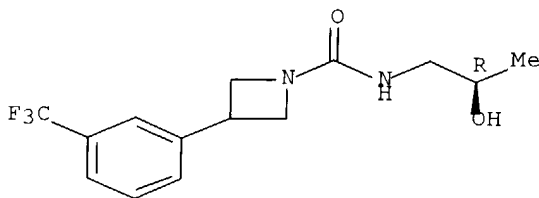
SR CA

LC STN Files: CA, CAPLUS

DT.CA Caplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 80 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN

RN 231953-65-4 REGISTRY

CN 1-Azetidinecarboxamide, 3-(3,4-dichlorophenyl)-N-[(2R)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

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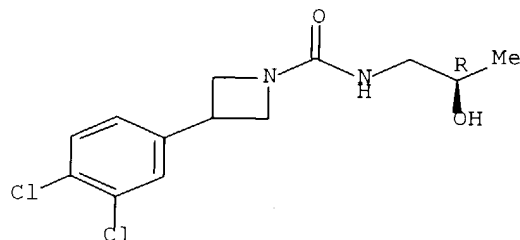
FS STEREOSEARCH

MF C13 H16 Cl2 N2 O2

Searched by P. Ruppel

SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 85 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231953-57-4 REGISTRY
CN 1-Azetidinecarboxamide, 3-(4-fluorophenyl)-N-[(2R)-2-hydroxypropyl]- (9CI)
(CA INDEX NAME)

OTHER NAMES:

CN (R)-3-(4-Fluorophenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

FS STEREOSEARCH

MF C13 H17 F N2 O2

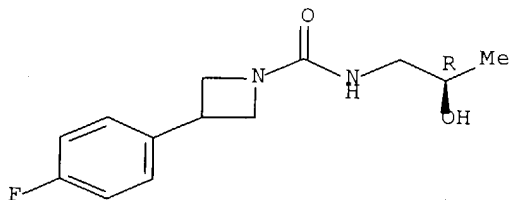
SR CA

LC STN Files: CA, CAPLUS

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 90 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN
RN 231953-49-4 REGISTRY

Searched by P. Ruppel

CN 1-Azetidinecarboxamide, 3-[4-(1,1-dimethylethyl)phenyl]-N-2-propenyl-
(9CI) (CA INDEX NAME)

OTHER NAMES:

CN 3-(4-tert-Butylphenyl)-N-(2-propenyl)azetidine-1-carboxamide

FS 3D CONCORD

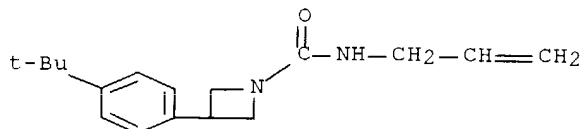
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LC STN Files: CA, CAPLUS

DT.CA CAplus document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES
(Uses)



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2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L35 ANSWER 95 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN

RN 97020-54-7 REGISTRY

CN 1-Azetidinecarboxamide, N-butyl-3-ethyl-2-oxo-3-phenyl- (7CI) (CA INDEX
NAME)

FS 3D CONCORD

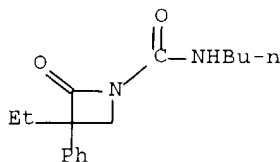
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LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS

(*File contains numerically searchable property data)

DT.CA CAplus document type: Journal

RL.NP Roles from non-patents: NORL (No role in record)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

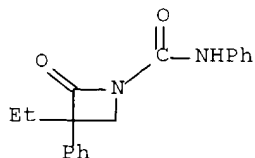
L35 ANSWER 100 OF 114 REGISTRY COPYRIGHT 2004 ACS on STN

RN 93879-35-7 REGISTRY

CN 1-Azetidinecarboxanilide, 3-ethyl-2-oxo-3-phenyl- (7CI) (CA INDEX NAME)

FS 3D CONCORD

MF C18 H18 N2 O2
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS
(*File contains numerically searchable property data)
DT.CA CAPLUS document type: Journal
RL.NP Roles from non-patents: NORL (No role in record)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> b zcaplus

FILE 'ZCAPLUS' ENTERED AT 11:50:06 ON 02 JUN 2004
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FILE COVERS 1907 - 2 Jun 2004 VOL 140 ISS 23
FILE LAST UPDATED: 1 Jun 2004 (20040601/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

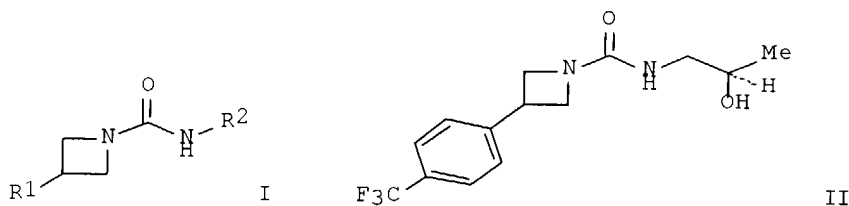
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L2 STR
L4 98 SEA FILE=REGISTRY SSS FUL L2
L32 STR
L34 33 SEA FILE=REGISTRY SSS FUL L32
L35 114 SEA FILE=REGISTRY ABB=ON PLU=ON L4 OR L34
L36 11 SEA FILE=ZCAPLUS ABB=ON PLU=ON L35
L37 10 SEA FILE=ZCAPLUS ABB=ON PLU=ON L36 AND (PRY<=1999 OR PY<=2002 OR AY<=2002)

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L37 ANSWER 1 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:78214 ZCAPLUS Full-text
 DN 134:147487
 ED Entered STN: 02 Feb 2001
 TI Preparation of azetidinecarboxamides for use as neuroprotectants
 IN Snape, Mike Frederick
 PA Vernalis Research Limited, UK
 SO PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 CC 27-5 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001007022	A2	20010201	WO 2000-GB2817	20000721 <--
	WO 2001007022	A3	20010614		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	EP 1196165	A2	20020417	EP 2000-946187	20000721 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
PRAI	GB 1999-17384	A	19990723 <--		
	WO 2000-GB2817	W	20000721		
OS	MARPAT 134:147487				
GI					



AB Syntheses of compds of formula I (85 examples) are described, wherein R1 is aryl; and R2 is H or alkyl; groups may be (un)saturated and/or (un)substituted; or a pharmaceutically acceptable salt or prodrug thereof. Compds. of formula I are candidates for neuroprotection or for the treatment of cerebral ischemia, central nervous system injury or eye diseases. Compound II was synthesized by addition of 4-(trifluoromethyl)phenyl magnesium bromide

to 1-(diphenylmethyl)-3-azetidinone followed by deoxygenation. The resulting aryl azetidine was protected as its N-diphenylmethyl derivative. The protected azetidine was then treated with phosgene and (R)-1-amino-2-propanol to provide II. Compound II exhibits neuroprotection at a dose of 30 mg/kg i.p. in the rat transient middle cerebral artery occlusion model measured by decrease in infarct volume

ST azetidinecarboxamide neuroprotectant prepn

IT Nervous system

(central, injury; preparation of azetidinecarboxamides for use as neuroprotectants)

IT Brain, disease

(ischemia; preparation of azetidinecarboxamides for use as neuroprotectants)

IT Cytoprotective agents

(neuroprotectants; preparation of azetidinecarboxamides for use as neuroprotectants)

IT Eye, disease

GABA agonists

(preparation of azetidinecarboxamides for use as neuroprotectants)

IT **231953-70-1P**, (R)-3-(4-Trifluoromethylphenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide **231954-58-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of azetidinecarboxamides for use as neuroprotectants)

IT **231953-45-0P**, 3-(4-Chlorophenyl)-N-(2-propenyl)azetidine-1-carboxamide **231953-49-4P**, 3-(4-tert-Butylphenyl)-N-(2-propenyl)azetidine-1-carboxamide **231953-50-7P**,

3-(4-tert-Butylphenyl)-N-(2-propynyl)azetidine-1-carboxamide

231953-51-8P, (R)-3-(4-tert-Butylphenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide **231953-55-2P**,

3-(4-Fluorophenyl)-N-(2-propenyl)azetidine-1-carboxamide

231953-56-3P, 3-(4-Fluorophenyl)-N-(2-propynyl)azetidine-1-carboxamide

231953-57-4P, (R)-3-(4-Fluorophenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

231953-58-5P,

3-(4-Chlorophenyl)-N-(2-propynyl)azetidine-1-carboxamide

231953-59-6P, (R)-3-(4-Chlorophenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

231953-60-9P, (S)-3-(4-Fluorophenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

231953-64-3P,

3-(3,4-Dichlorophenyl)-N-(2-propynyl)azetidine-1-carboxamide

231953-65-4P, (R)-3-(3,4-Dichlorophenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

231953-66-5P,

(S)-3-(3,4-Dichlorophenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

231953-71-2P, (S)-3-(4-Trifluoromethylphenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

231953-72-3P,

3-(4-Trifluoromethylphenyl)-N-(2-propynyl)azetidine-1-carboxamide

231953-76-7P, (R)-3-(3-Trifluoromethylphenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

231953-77-8P,

(S)-3-(3-Trifluoromethylphenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

231953-78-9P, 3-(3-Trifluoromethylphenyl)-N-(2-propynyl)azetidine-1-carboxamide

231953-79-0P, 3-(4-Trifluoromethylphenyl)-N-

azetidine-1-carboxamide **231953-80-3P** **231953-81-4P**

231953-82-5P **231953-83-6P** **231953-84-7P**

231953-85-8P **231953-86-9P** **231953-87-0P**

231953-88-1P **231953-89-2P** **231953-90-5P**

231953-91-6P **231953-92-7P** **231953-94-9P**

231953-95-0P **231953-97-2P** **231953-99-4P**

231954-02-2P **231954-04-4P** **231954-06-6P**

231954-08-8P **231954-12-4P** **231954-13-5P**

231954-14-6P 231954-16-8P 231954-18-0P
 231954-20-4P 231954-21-5P 231954-23-7P
 231954-25-9P 231954-27-1P 231954-29-3P
 231954-31-7P 231954-32-8P 231954-34-0P
 231954-35-1P 231954-36-2P 231954-37-3P
 231954-38-4P 231954-39-5P 231954-40-8P
 231954-41-9P 231954-42-0P 231954-43-1P
 231954-44-2P 231954-45-3P 231954-46-4P
 231954-47-5P 231954-48-6P 231954-49-7P
 231954-50-0P 231954-51-1P 231954-52-2P
 231954-53-3P 231954-55-5P 231954-56-6P
 231954-59-9P 231954-60-2P 231954-61-3P
 231955-16-1P 323204-84-8P 323204-85-9P
 323204-86-0P 323204-87-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of azetidinecarboxamides for use as neuroprotectants)

IT 107-11-9, Allylamine 352-13-6, 4-Fluorophenylmagnesium bromide
 402-26-6, 3-(Trifluoromethyl)phenylmagnesium bromide 402-51-7,
 4-(Trifluoromethyl)phenylmagnesium bromide 688-73-3, Tributyltin hydride
 873-77-8, 4-Chlorophenylmagnesium bromide 1476-23-9, Allyl isocyanate
 2450-71-7, Propargylamine 2799-16-8, (R)-1-Amino-2-propanol 2799-17-9,
 (S)-1-Amino-2-propanol 18621-17-5, 1-(Diphenylmethyl)-3-azetidinol
 63488-10-8, 4-tert-Butylphenylmagnesium bromide 79175-35-2,
 3,4-Dichlorophenylmagnesium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of azetidinecarboxamides for use as neuroprotectants)

IT 7606-31-7P, 3-(4-Chlorophenyl)azetidine hydrochloride 40320-60-3P,
 1-Diphenylmethyl-3-azetidinone 231953-42-7P 231953-43-8P
 231953-44-9P, 3-(4-Chlorophenyl)-1-(diphenylmethyl)azetidine
 231953-46-1P 231953-47-2P, 3-(4-tert-Butylphenyl)-3-chloro-1-
 (diphenylmethyl)azetidine 231953-48-3P, 3-(4-tert-Butylphenyl)-1-
 (diphenylmethyl)azetidine 231953-52-9P 231953-53-0P,
 3-(4-Fluorophenyl)-3-chloro-1-(diphenylmethyl)azetidine 231953-54-1P,
 3-(4-Fluorophenyl)-1-(diphenylmethyl)azetidine 231953-63-2P
 231953-69-8P, 3-(4-(Trifluoromethyl)phenyl)-1-(diphenylmethyl)azetidine
 231953-75-6P, 3-(3-(Trifluoromethyl)phenyl)-1-(diphenylmethyl)azetidine
 231954-62-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthetic intermediate; preparation of azetidinecarboxamides for use as neuroprotectants)

IT 231953-70-1P, (R)-3-(4-Trifluoromethylphenyl)-N-(2-hydroxypropyl)azetidine-1-carboxamide

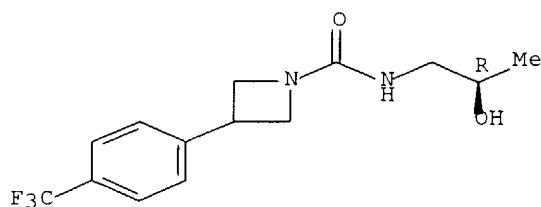
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of azetidinecarboxamides for use as neuroprotectants)

RN 231953-70-1 ZCAPLUS

CN 1-Azetidinecarboxamide, N-[(2R)-2-hydroxypropyl]-3-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

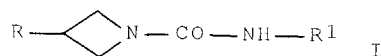
Absolute stereochemistry.



L37 ANSWER 2 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:487270 ZCAPLUS Full-text
 DN 131:102183
 ED Entered STN: 06 Aug 1999
 TI Azetidinecarboxamide derivatives for treating CNS disorders
 IN Shepherd, Robin Gerald; Adams, David Reginald; Bentley, Jon; Bodkin, Corinna Dagmar; Cliffe, Ian Anthony; Davidson, James Edward Paul; Mansell, Howard Langham; Monck, Nathaniel Julius
 PA Cerebrus Limited, UK; Shepherd, Joy, Miriam
 SO PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07D205-04
 ICS A61K031-395
 CC 27-5 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9937613	A1	19990729	WO 1999-GB223	19990122	<--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9921780	A1	19990809	AU 1999-21780	19990122	<--
	EP 1049670	A1	20001108	EP 1999-901781	19990122	<--
	EP 1049670	B1	20020717			
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002501046	T2	20020115	JP 2000-528537	19990122	<--
	AT 220665	E	20020815	AT 1999-901781	19990122	<--
	PT 1049670	T	20021231	PT 1999-901781	19990122	<--
	ES 2181387	T3	20030216	ES 1999-901781	19990122	<--
PRAI	GB 1998-1499	A	19980123			<--
	GB 1998-24458	A	19981106			<--
	WO 1999-GB223	W	19990122			<--
OS	MARPAT 131:102183					
GI						



- AB Title compd. I (R is aryl; and R1 is H or alkyl); pharmaceutically acceptable addition compds. thereof; and their use in therapy, particularly for the treatment and prophylaxis of CNS disorders such as anxiety and epilepsy is covered. 3-(4-Fluorophenyl)-1-(diphenylmethyl)azetidine (II), prepared by Grignard reaction of 1-(diphenylmethyl)-3-azetidinone with 4-fluorophenylmagnesium bromide followed by dechlorination, was treated with phosgene followed by allylamine, propargylamine or (R)-1-amino-2-propanol to give I [R = p-FC6H4, R1 = allyl, propargyl (III), CH2CH(OH)Me-(R), resp.]. Among the approx. 40 azetidines similarly prepared were I [R = p-ClC6H4, p-t-BuC6H4, 3,4-Cl2C6H3, m-, p-F3CC6H4; R1 = same as above, CH2CH(OH)Me-(S)]. Azetidine III was an effective anxiolytic at a dose of 100 mg/Kg in the rat.
- ST azetidinecarboxamide anxiolytic anticonvulsant prepn
- IT Anticonvulsants
Anxiolytics
(azetidinecarboxamides)
- IT **231953-45-0P 231953-49-4P 231953-50-7P**
231953-51-8P 231953-55-2P 231953-56-3P
231953-57-4P 231953-58-5P 231953-59-6P
231953-60-9P 231953-71-2P 231953-78-9P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation and anti-anxiety and anti-epileptic activity of azetidinecarboxamides)
- IT **231953-80-3 231953-81-4 231953-82-5**
231953-83-6 231953-84-7 231953-85-8
231953-86-9 231953-87-0 231953-88-1
231953-89-2 231953-90-5 231953-91-6
231953-92-7 231953-94-9 231953-95-0
231953-97-2 231953-99-4 231954-02-2
231954-04-4 231954-06-6 231954-08-8
231954-10-2 231954-12-4 231954-13-5
231954-14-6 231954-16-8 231954-18-0
231954-20-4 231954-21-5 231954-23-7
231954-25-9 231954-27-1 231954-29-3
231954-31-7 231954-32-8 231954-34-0
231954-35-1 231954-36-2 231954-37-3
231954-38-4 231954-39-5 231954-40-8
231954-41-9 231954-42-0 231954-43-1
231954-44-2 231954-45-3 231954-46-4
231954-47-5 231954-48-6 231954-49-7
231954-50-0 231954-51-1 231954-52-2
231954-53-3 231954-54-4 231954-55-5
231954-56-6 231954-57-7 231954-58-8
231954-59-9 231954-60-2 231954-61-3
231955-16-1
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
 (preparation and anti-anxiety and anti-epileptic activity of azetidinecarboxamides)
- IT 107-11-9, Allylamine 352-13-6, 4-Fluorophenylmagnesium bromide
 873-77-8, 4-Chlorophenylmagnesium bromide 1476-23-9, Allyl isocyanate
 2450-71-7, Propargylamine 2799-16-8, (R)-1-Amino-2-propanol
 63488-10-8, 4-tert-Butylphenylmagnesium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and anti-anxiety and anti-epileptic activity of
azetidinecarboxamides)

IT 7215-02-3P, 3-(4-Chlorophenyl)azetidine 7606-31-7P, 3-(4-Chlorophenyl)azetidine hydrochloride 18621-17-5P, 1-(Diphenylmethyl)-3-azetidinol 40320-60-3P, 1-(Diphenylmethyl)-3-azetidinone 231953-42-7P
231953-43-8P 231953-44-9P 231953-46-1P 231953-47-2P 231953-48-3P
231953-52-9P 231953-53-0P 231953-54-1P 231953-61-0P 231953-62-1P
231953-63-2P 231953-67-6P 231953-68-7P 231953-69-8P 231953-74-5P
231953-75-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and anti-anxiety and anti-epileptic activity of
azetidinecarboxamides)

IT 402-26-6P, 3-(Trifluoromethyl)phenylmagnesium bromide 402-51-7P,
4-(Trifluoromethyl)phenylmagnesium bromide 2799-17-9P,
(S)-1-Amino-2-propanol 79175-35-2P, 3,4-Dichlorophenylmagnesium bromide
231953-64-3P 231953-65-4P 231953-66-5P
231953-70-1P 231953-72-3P 231953-73-4P
231953-76-7P 231953-77-8P 231953-79-0P
231954-62-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and anti-anxiety and anti-epileptic activity of
azetidinecarboxamides)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

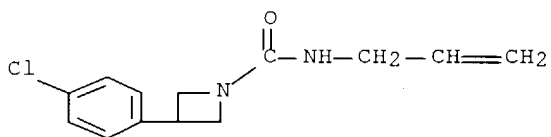
- (1) Lepetit S P A; GB 872447 A 1961 ZCAPLUS
- (2) Robins Co Inc A H
- (3) Robins Co Inc A H; EP 0194112 A 1986 ZCAPLUS

IT **231953-45-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anti-anxiety and anti-epileptic activity of
azetidinecarboxamides)

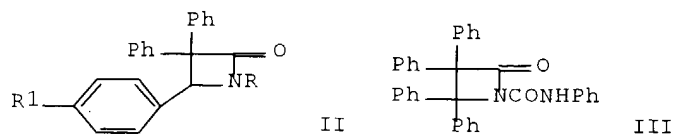
RN 231953-45-0 ZCAPLUS

CN 1-Azetidinecarboxamide, 3-(4-chlorophenyl)-N-2-propenyl- (9CI) (CA INDEX NAME)



L37 ANSWER 3 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN
AN 1981:515162 ZCAPLUS Full-text
DN 95:115162
ED Entered STN: 12 May 1984
TI Syntheses of N-substituted 3,3,4-triaryl- and 3,3,4,4-tetraphenyl-2-azetidinones
AU Mehrotra, Kailash Nath; Singh, Surendra Bahadur
CS Dep. Chem., Banaras Hindu Univ., Varanasi, 221005, India
SO Bulletin of the Chemical Society of Japan (1981), 54(6), 1838-40
CODEN: BCSJA8; ISSN: 0009-2673
DT Journal

LA English
 CC 27-5 (Heterocyclic Compounds (One Hetero Atom))
 OS CASREACT 95:115162
 GI



AB The reactions of $N_2CPhCOPh$ (I) with $RCH:NHC_6H_4R_1$ ($R = Me_2CH, Ph_2CH, MePhCH$; $R_1 = H, 4-MeO, 4-Cl, 4-NO_2, 4-Me_2N$) gave 2-azetidinones II together with 1,1',4,4'-tetraphenyl-2,2'-azinodiethanone. I reacts with $Ph_2C:NCONHPh$ to give III.

ST diazoethanone Schiff base cycloaddn; azetidinone phenyl

IT Cycloaddition reaction
 (of diazoethanone with Schiff bases)

IT 3469-17-8
 RL: PROC (Process)
 (cycloaddn. of, with Schiff bases)

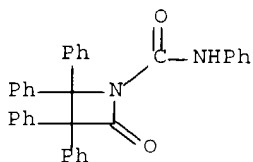
IT 3129-98-4 6852-56-8 40462-63-3 40462-76-8 40462-77-9 62506-88-1
 66607-69-0
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (cycloaddn. with diazodiphenylethanone)

IT 3893-33-2P 23490-87-1P 76876-94-3P 78846-92-1P 78846-93-2P
 78846-94-3P 78846-95-4P 78846-96-5P 78846-97-6P **78846-98-7P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

IT **78846-98-7P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

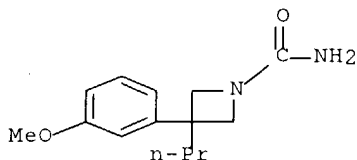
RN 78846-98-7 ZCAPLUS

CN 1-Azetidinecarboxamide, 4-oxo-N,2,2,3,3-pentaphenyl- (9CI) (CA INDEX NAME)



L37 ANSWER 4 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1968:435829 ZCAPLUS Full-text
 DN 69:35829
 ED Entered STN: 12 May 1984
 TI Analgetics based on the azetidine ring
 AU Bishop, D. C.; Cavalla, J. F.; Lockhart, I. M.; Wright, M.; Winder, C. V.;

Wong, A.; Stephens, M.
 CS Parke, Davis and Co., Hounslow, UK
 SO Journal of Medicinal Chemistry (1968), 11(3), 466-70
 CODEN: JMCMAR; ISSN: 0022-2623
 DT Journal
 LA English
 CC 27 (Heterocyclic Compounds (One Hetero Atom))
 OS CASREACT 69:35829
 GI For diagram(s), see printed CA Issue.
 AB A series of azetidines (I) has been synthesized and examd. for analgetic activity. The activity is comparable with that of pyrrolidines prepared previously. Relative activities within the azetidine series do not, however, closely parallel those of the corresponding pyrrolidines.
 ST analgetics azetidines; azetidines analgetics
 IT Analgesics
 (azetidine derivs. as)
 IT 17184-83-7P 17184-85-9P 17184-86-0P 19832-16-7P 19832-17-8P
 19832-18-9P 19832-19-0P 19832-20-3P 19832-21-4P 19832-22-5P
 19832-23-6P 19832-24-7P 19832-25-8P 19832-26-9P 19832-27-0P
 19832-28-1P 19832-29-2P 19832-30-5P 19832-31-6P 19832-32-7P
 19832-33-8P 19832-36-1P 19832-37-2P 19832-38-3P 19832-39-4P
 19832-40-7P 19832-41-8P 19832-42-9P 19832-43-0P 19832-44-1P
 19832-45-2P 19832-46-3P 19832-47-4P 19832-48-5P 19832-49-6P
19832-50-9P 19832-51-0P 19832-52-1P 19832-53-2P
 19857-64-8P 19857-65-9P 19857-66-0P 20051-69-8P 20061-96-5P
 20061-97-6P 20061-98-7P 20061-99-8P 20062-00-4P 20062-01-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 IT **19832-50-9P**
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 19832-50-9 ZCAPLUS
 CN 1-Azetidinecarboxamide, 3-(m-methoxyphenyl)-3-propyl- (8CI) (CA INDEX NAME)



L37 ANSWER 5 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1964:60733 ZCAPLUS Full-text
 DN 60:60733
 OREF 60:10626b-h,10627a-d
 ED Entered STN: 22 Apr 2001
 TI Substances acting on the central nervous system. XXXIII.
 3-Hydroxymethyl-3-phenylazetidine and derivatives
 AU Testa, Emilio; Fontanella, Luigi; Bovara, Mario
 CS Lepetit S.p.A., Milan
 SO (1964) 97-106
 DT Journal
 LA Unavailable
 CC 37 (Heterocyclic Compounds (One Hetero Atom))

OS CASREACT 60:60733

GI For diagram(s), see printed CA Issue.

AB cf. CA 59, 12735h; 60, 6847f. I ($R = R' = H$) (II) and a no. of its derivs. were prepared for pharmacol. investigation. To a suspension of 32 g. $LiAlH_4$ in 500 cc. tetrahydrofuran (THF) was added slowly dropwise at below 20° a 10% solution of 38 g. 3-hydroxymethyl-3-phenyl-2-azetidinone (IIa) in THF and the mixture refluxed 8 hrs. to give 17.85 g. II, m. $135-7^\circ$ (EtOAc); HCl salt m. $211-12^\circ$ (EtOH). Phthalimide (2.26 g.) in 40 cc. 95% EtOH heated 5 min. at $60-70^\circ$ with 4.39 cc. 39% aqueous HCHO, the solution treated dropwise at $60-70^\circ$ with 2.5 g. II in 35 cc. EtOH, boiled 30 min., filtered hot, and concentrated in vacuo, the oily residue dissolved in 100 cc. absolute Et₂O, and the solution filtered and treated with saturated Et₂O-HCl gave 3.08 g. I ($R =$ phthalimidomethyl, $R' = H$) HCl salt, m. $165-7^\circ$ (EtOH). 3,3-Diisopropyl-2,4-azetidinedione (3.1 g.), 35 cc. EtOH, 1.8 cc. 39% aqueous HCHO, and 3 g. II in 60 cc. EtOH treated similarly gave 6.1 g. I ($R = 3,3$ -diisopropyl-2,4-dioxazetidinylmethyl, $R' = H$), m. $90-2^\circ$ (aqueous EtOH). II.HCl (2 g.) and 650 mg. NaOCN in 20 cc. H₂O heated 15 min. at 60° and refrigerated overnight gave 1.5 g. I ($R = CONH_2$, $R' = H$) (III), m. $180-2^\circ$ (absolute EtOH). III (900 mg.) in 25 cc. CHCl₃ treated at 0° with stirring with 400 mg. NaOCN under anhydrous conditions followed by dry HCl (1 hr.) and 400 mg. NaOCN added followed by dry HCl (1 hr.) gave 120 mg. I ($R = R' = CONH_2$), m. 2213° (H₂O). II (2 g.) in 30 cc. absolute PhMe treated dropwise with 2.8 g. PhNCO, and the mixture heated 15 min. at 50° and cooled to 0° gave 3.1 g. I ($R = CONHPh$, $R' = H$), m. $211-12^\circ$ (absolute EtOH). II (10 g.) dissolved in 60 cc. cold N H₂SO₄, the solution treated gradually at $0-5^\circ$ with 5.4 g. NaNO₂ with stirring, let warm up slowly, heated 30 min. on a water bath, treated with 2 g. NaNO₂, boiled 15 min., and cooled, and the product isolated with EtOAc-Et₂O gave 7 g. I ($R = NO$, $R' = H$) (IV), m. $72-5^\circ$ (Et₂O). To a cold ($0-5^\circ$) suspension of 580 mg. $LiAlH_4$ in 20 cc. THF was added slowly 2 g. IV in 20 cc. THF with stirring and the mixture heated slowly to 45° and stirred 2 hrs, at 45° to give 660 mg. I ($R = NH_2$, $R' = H$), m. $109-12^\circ$ (EtOAc); p-nitrobenzylidene derivative m. $122-3^\circ$ (absolute EtOH). To a suspension of 2 g. II.HCl in 10 cc. AcOH was added 1.1 cc. AcCl at 20° and the mixture let stand 24 hrs. to give 2.1 g. I ($R = H$, $R' = Ac$) HCl salt, m. $145-7^\circ$ (MeOH-Et₂O), (Method A) II (2.5 g.) in 5 cc. pyridine treated dropwise with 2.5 cc. (EtCO)₂O (V) with icesalt cooling, the solution let warm up slowly, kept overnight at 20° , diluted with 15 cc. EtOH, boiled 15 min., and evaporated in vacuo, the residue dissolved in 2N HCl, the solution extracted with Et₂O, and the extracted distilled gave 1.7 g. I ($R = R' = EtCO$) (VI), b.p. $175-85^\circ$ (air bath). (Method B) II (3.5 g.) and 10 cc. V heated 30 min. at 130° and the mixture cooled to 80° , diluted with 30 cc. EtOH, heated 30 min. at $80-90^\circ$, and then processed by method A gave 4.34 g. VI, b.p. $175-85^\circ$ (air bath). From II and Ac₂O was prepared by method B 71% I ($R = R' = Ac$) (VII), m. $104-5^\circ$ (Et₂O). From II and BzCl was prepared by method A 74% I ($R = R' = Bz$) (VIIa), m. $98-100^\circ$ (Et₂O). VII (7.9 g.) in 13 cc. MeOH kept overnight at 20° with 13 cc. 10% aqueous KOH, the solution evaporated in vacuo, the residue extracted with EtOAc, and the extract concentrated to small volume deposited 5.01 g. I ($R = Ac$, $R' = H$) (VIII), m. $119-21^\circ$ (EtOAc). Crude II (obtained by reduction of 109 g. IIa with 65 g. $LiAlH_4$) dissolved in 10% HCl, and the solution extracted with EtOAc and made alkaline with 50% aqueous NaOH gave 66 g. VIII, m. $120-1^\circ$ (EtOAc). VIII (1.16 g.) in 25 cc. 10% HCl refluxed 45 min., the solution evaporated in vacuo, and the residual solid repeatedly evaporated with EtOH gave 1.05 g. II.HCl, m. $210-12^\circ$ (EtOH). VI hydrolyzed like VII gave 91% I ($R = Pr$, $R' = H$), m. $76-7^\circ$ (Et₂O). II (4 g.) dissolved in 2.26 g. HCO₂H under cooling after 2 min. 800 mg. 35% aqueous HCHO added, followed by 4 cc. H₂O, the solution heated slowly, boiled 2 hrs., treated with 6 cc. 12N HCl at the b.p., and after 5 min. concentrated in vacuo, and the residual oil repeatedly evaporated with MeOH and crystallized from MeOH-Et₂O gave 1.2 g. I ($R = Me$, $R' = H$) HCl salt (IX.HCl), m. $151-3^\circ$ (EtOH-Et₂O); IX m. $96-7^\circ$ (sublimation at $60^\circ/2$ mm.); picrate m. 1579° (EtOH) methiodide, m. $182-3^\circ$ (Et₂O). To a suspension of 1 g.

LiAlH₄ in 50 cc. Et₂O was added dropwise 1.5 g. VII in 100 cc. Et₂O with stirring and cooling and the mixture slowly brought to the b.p. and refluxed 3 hrs. to give 1.05 g. I (R = Et, R' = H) (IXa), m. 90-1° (Et₂O); HCl salt m. 158° (EtOH-Et₂O); picrate m. 125-7° (EtOH); methiodide m. 113-15° (Et₂O). To a stirred suspension of 15 g. LiAlH₄ in 200 cc. Et₂O was added dropwise 21 g. VIIa in 400 cc. Et₂O with cooling to give 14.6 g. I (R = PhCH₂, R' = H) HCl salt (X.HCl), m. 148-50°, which (500 mg.) was dissolved in 10 cc. cold H₂O and treated with N NaOH to give 355 mg. X, m. 89-91° (C₆H₆-petr. ether); methiodide, m. 143° (Me₂CO-Et₂O). Very finely powdered NaOCN (1.2 g.) added to 3 g. IX in 50 cc. dry CHCl₃ at 0° (anhydrous conditions), the mixture treated with dry HCl at 0°, treated with 1.2 g. finely powdered NaOCN, followed by dry HCl for 1 hr., stirred 1 hr. at 0°, and extracted with H₂O, and the aqueous solution extracted with EtOAc and made alkaline with N NaOH under cooling gave 2.4 g. I (R = Me, R' = H₂NOC), m. 119-22° (Et₂O). From IXa and X and NaO-CN were similarly prepared 67% I (R = Et, R' = H₂NOC), m. 93-5° (methiodide m. 177-8°), and 63% I (R = PhCH₂, R' = H₂NOC), m. 101-2° (Et₂O), resp. IX.HCl (3.5 g.) in 15 cc. AcOH treated slowly with 2.15 cc. EtCOCl and the solution let stand 24 hrs. gave 3.15 g. I (R = Me, R' = EtCO) HCl salt (XI.HCl), m. 149-51° (Me₂CO); XI, viscous oil, b_{0.2} 80-5° (air bath). IXa and X treated similarly with EtCOCl gave 79% I (R = Et, R' = EtCO) HCl salt, m. 155-7° (Me₂CO), and 61% I (R = PhCH₂, R' = EtCO), b_{0.4} 160° (air bath) [picrate m. 125-7° (Et₂O); H maleate m. 140-2° (EtOAc)], resp. IXa (3 g.) in 9 cc. Ac₂O heated 30 min. at 120°, the solution cooled to 80°, treated with 20 cc. EtOH, boiled 15 min., and evaporated in vacuo, and the residue extracted with Et₂O gave 2.95 g. AcNEtCH₂CPh-(CH₂OAc)₂ (XII), m. 79-80° (iso-Pr₂O). XII (3.3 g.) in 50 cc. 10% HCl refluxed 45 min. gave 1.2 g. (HOH₂C)₂CPhCH₂NH-Et. HCl (XIII.HCl), m. 116-18°. To a suspension of 12 g. Li-AlH₄ in 150 cc. Et₂O was added dropwise 18 g. AcHNCH₂CPh (CH₂OH)CO₂Et in 250 cc. Et₂O with stirring and cooling and the mixture boiled 6 hrs. to give 9.7 g. XIII, b_{0.2} 140-5° (air bath), converted to 5.9 g. XIII.HCl, m. 116-18° (Me₂CO).

- IT Nervous system
 (effect of 3-phenyl-3-azetidinemethanol and derivs. on central)
- IT 1-Azetidinecarboxamide, 3-(hydroxymethyl)-3-phenyl-, carbamate
 3-Azetidinemethanol, 1-benzyl-3-phenyl-, carbamate
 3-Azetidinemethanol, 1-ethyl-3-phenyl-, carbamate
 3-Azetidinemethanol, 1-ethyl-3-phenyl-, propionate, hydrochloride
 3-Azetidinemethanol, 1-methyl-3-phenyl-, carbamate
 Azetidinium compounds, 1-benzyl-3-(hydroxymethyl)-1-methyl-3-phenyl-, iodide
 Azetidinium compounds, 1-ethyl-3-(hydroxymethyl)-1-methyl-3-phenyl-, iodide
 Azetidinium compounds, 1-ethyl-3-(hydroxymethyl)-1-methyl-3-phenyl-, iodide, carbamate
 Azetidinium compounds, 3-(hydroxymethyl)-1,1-dimethyl-3-phenyl-, iodide
 Carbamic acid (aminoformic acid), (1-benzyl-3-phenyl-3-azetidiny)methyl ester
 Carbamic acid (aminoformic acid), (1-ethyl-3-phenyl-3-azetidiny)methyl ester
 Carbamic acid (aminoformic acid), (1-methyl-3-phenyl-3-azetidiny)methyl ester
 Carbamic acid (aminoformic acid), esters with 1-ethyl-3-(hydroxymethyl)-1-methyl-3-phenylazetidinium iodide
 Carbamic acid (aminoformic acid), esters with 3-(hydroxymethyl)-3-phenyl-1-azetidinecarboxamide
- IT 1017-58-9, 2-Furaldehyde, 5,5'-thiodi- 5961-34-2, 3-Azetidinemethanol, 3-phenyl- 22627-22-1, 3-Azetidinemethanol, 1-methyl-3-phenyl- 25566-04-5, 3-Azetidinol, 3-phenyl- 74039-95-5, 3-Azetidinemethanol, 1-acetyl-3-phenyl- 77184-08-8, 2-Azetidinone, 3-hydroxy-3-phenyl- 90872-90-5, 3-Azetidinemethanol, 1-amino-3-phenyl- 90874-63-8, 3-Azetidinemethanol, 3-phenyl-, hydrochloride 90918-06-2,

3-Azetidinemethanol, 1-nitroso-3-phenyl- **91180-96-0**,
 1-Azetidinecarboxamide, 3-(hydroxymethyl)-3-phenyl- 91554-36-8,
 1,3-Propanediol, 2-[(ethylamino)methyl]-2-phenyl-, hydrochloride
 91554-37-9, 1,3-Propanediol, 2-[(ethylamino)methyl]-2-phenyl-
 91562-74-2, 3-Azetidinemethanol, 1-ethyl-3-phenyl-, hydrochloride
 91562-75-3, 3-Azetidinemethanol, 1-ethyl-3-phenyl- 91640-43-6,
 3-Azetidinemethanol, 3-phenyl-, acetate, hydrochloride 92040-44-3,
 3-Azetidinemethanol, 3-phenyl-1-propionyl- 92146-70-8,
 3-Azetidinemethanol, 1-methyl-3-phenyl-, hydrochloride 92245-96-0,
 3-Azetidinemethanol, 1-acetyl-3-phenyl-, acetate 92500-20-4,
 3-Azetidinemethanol, 1-methyl-3-phenyl-, propionate, hydrochloride
 92500-21-5, 3-Azetidinemethanol, 1-methyl-3-phenyl-, propionate
 93025-34-4, 3-Azetidinemethanol, 3-phenyl-1-propionyl-, propionate
 93406-09-8, 3-Azetidinemethanol, 1-benzyl-3-phenyl-, hydrochloride
 93406-10-1, 3-Azetidinemethanol, 1-benzyl-3-phenyl- **93649-10-6**,
 1-Azetidinecarboxanilide, 3-(hydroxymethyl)-3-phenyl- 93650-94-3,
 3-Azetidinemethanol, 1-methyl-3-phenyl-, picrate 94069-42-8,
 3-Azetidinemethanol, 1-ethyl-3-phenyl-, picrate 94576-28-0,
 3-Azetidinemethanol, 1-benzyl-3-phenyl-, propionate 94959-90-7,
 3-Azetidinemethanol, 1-[(p-nitrobenzylidene)amino]-3-phenyl- 94982-51-1,
 3-Azetidinol, 3-phenyl-, hydrogen oxalate 95364-38-8, Formamide,
 N-[β,β-bis(hydroxymethyl)phenethyl]-N-ethyl-, diacetate
 95696-95-0, Malonimide, N-[[3-(hydroxymethyl)-3-phenyl-1-
 azetidiny]methyl]-2,2-diisopropyl- 95704-72-6, 3-Azetidinemethanol,
 1-benzoyl-3-phenyl-, benzoate 98800-93-2, Phthalimide,
 N-[[3-(hydroxymethyl)-3-phenyl-1-azetidiny]methyl]-, hydrochloride
 101941-32-6, 3-Azetidinemethanol, 1-benzyl-3-phenyl-, propionate, H
 maleate 103241-72-1, 3-Azetidinemethanol, 1-benzyl-3-phenyl-,
 propionate, picrate

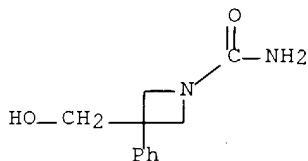
(preparation of)

IT **91180-96-0**, 1-Azetidinecarboxamide, 3-(hydroxymethyl)-3-phenyl-

(preparation of)

RN 91180-96-0 ZCAPLUS

CN 1-Azetidinecarboxamide, 3-(hydroxymethyl)-3-phenyl- (7CI) (CA INDEX NAME)



L37 ANSWER 6 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN

AN 1963:415448 ZCAPLUS Full-text

DN 59:15448

OREF 59:2745e-h,2746b-h

ED Entered STN: 22 Apr 2001

TI Substances acting on the central nervous system. XXVI. Chemistry of
 3,3-disubstituted azetidines. 3.

AU Testa, Emilio; Fontanella, Luigi; Mariani, Luigi

CS Lepetit S.p.A., Milan, Italy

SO Ann. (1962), 660, 135-43

DT Journal

LA Unavailable

CC 37 (Heterocyclic Compounds (One Hetero Atom))

OS CASREACT 59:15448

GI For diagram(s), see printed CA Issue.

AB cf. CA 55, 6460a, 27270i; 59, 1521c. Derivs. of azetidine (I) were prepd. ClCH₂CH₂COCl (9.8 g.), 17 g. Et₃N (II), and 12.5 g. 3-phenyl-3-ethylazetidine (III) in 30 cc. absolute Et₂O at 0-5°, held 1 hr. at 0°, and acidified with cold dilute HCl yielded on isolation 14 g. crude N-(β-chloropropionyl)-3-phenyl-3-ethylazetidine (IV) (decomposed on distillation), which on refluxing 4 hrs. with 4.42 g. Et₂NH and 11.2 g. II in 30 cc. absolute C₆H₆, yielded on isolation an oil. The oil was taken up in Et₂O, decolorized with C, and treated with citric acid in Et₂O to give a precipitate of 15.2 g. N-(β-diethylaminopropionyl)-3-phenyl-3-ethylazetidine citrate, m. 142° (EtOAc-MeOH). IV (14 g.), 4.85 g. morpholine, 11.2 g. II, and 30 cc. absolute C₆H₆ was refluxed 4 hrs. and similarly gave an Et₂O solution, which with gaseous HCl yielded 9.3 g. N-(β-morpholinopropionyl)-3-phenyl-3-ethylazetidine hydrochloride, m. 165-8° (EtOAc-MeOH). MeCH(OAc)COCl (9.33 g.) slowly added to a solution of 10 g. III and 12.5 g. II in 30 cc. absolute C₆H₆ at 0° and after 2 hrs. poured into ice water yielded on isolation an oil. Hydrolysis of the oil by refluxing 30 min. with 170 cc. saturated NaHCO₃ and 170 cc. MeOH gave 7.1 g. N-(α-hydroxypropionyl)-3-phenyl-3-ethylazetidine, m. 79-81° (ligroine). 3-Phenyl-3-isopropylazetidine (7 g.) was treated with cooling with 21 cc. (EtCO)₂O (V), heated 60 min. at 115-20°, cooled to 60°, poured into 150 cc. lukewarm H₂O, cooled to 0° adjusted to pH 8-9, extracted with Et₂O, washed with 10% NaOH and then H₂O to yield 90% N-propionyl-3-phenyl-3-isopropylazetidine, b_{0.4} 140°. Reaction of 5 g. 3-phenyl-3-butylazetidine with V similarly gave 89% N-propionyl-3-phenyl-3-butylazetidine, b_{0.6} 150°. NaOEt from 23 g. Na and 100 cc. absolute EtOH in 350 cc. absolute PhMe, 117 g. PhCH₂CN, and 236 g. (EtO)₂CO (VI) was distilled slowly until the b.p. reached 110-12°, the residue cooled to 40°, 136 g. Et₂NCH₂CH₂Cl and 250 cc. absolute EtOH added, refluxed 90 min., evapd, in vacuo to 300 cc., 200 cc. H₂O added, extracted with Et₂O, the Et₂O extract washed with 10% NaOH and then H₂O to yield on distillation 250 g. ethyl α-phenyl-α-(β-diethylaminoethyl)-α-cyanoacetate, b_{1.5} 147-51° (VII). VII (150 g.) was reduced with H at 50 atmospheric in 250 cc. absolute EtOH and 70 g. Raney Ni at 70-80° to yield on isolation and distillation 70% ethyl α-phenyl-α-(β-diethylaminoethyl)-β-aminopropionate (VIII), b_{0.3} 134-6°. VIII (140 g.) in 280 cc. absolute Et₂O was dropped into a Grignard solution (from 42 g. Mg, 250 g. MeI, and 720 cc. absolute Et₂O) at 20-5°, after 1 hr. cooled to 0-5°, and acidified. The aqueous layer was alkalinized with 10% NaOH, filtered, and extracted with Et₂O to give on distillation 16% 3-phenyl-3-(β-diethylaminoethyl)azetidin-2-one (IX), b_{0.4} 138-45°. IX (10.9 g.) and 6.4 g. LiAlH₄ in absolute Et₂O was refluxed 4 hrs., cooled to 0°, treated with 50 cc. 20% NH₄Cl solution, followed by isolation and distn, of the product yielded 31% 3-phenyl-3-(β-diethylaminoethyl)azetidine (X), b_{0.4} 125-30°. X (3.1 g.) and 6.5 g. V were allowed to react and the product isolated to yield 20% N-propionyl-3-phenyl-3-(β-diethylaminoethyl)azetidine, b_{0.4} 160-5°. p-MeC₆H₄CH₂CN (111 g.) added to a solution of Na-OEt from 19.5 g. Na and 76 cc. absolute EtOH in 300 cc. absolute PhMe at 50°, 200 cc. VI and 50 cc. absolute PhMe added, the solution slowly distilled 4 hrs. until the b.p. reached 110°, cooled to 40°, and 120 g. EtBr (XI) in 210 cc. absolute EtOH added, the mixture refluxed 2-3 hrs. (to a neutral reaction), EtOH removed in vacuo, the residue treated with H₂O, and the product isolated by extraction and distillation gave 82% Et α-p-tolyl-α-ethyl-α-cyanoacetate (XII), b_{1.5} 129-31°. XII (148 g.) in 300 cc. absolute EtOH reduced with H and Raney Ni at 60 atmospheric and 70° gave 73% Et α-p-tolyl-α-ethyl-β-aminopropionate (XIII), b_{0.8} 118-22°; picrate m. 165-8° (EtOH). XIII (110.5 g.) in 300 cc. absolute Et₂O slowly stirred into 1 l. Grignard solution (36.5 g. Mg, 165 g. XI) at 0-5°, stirred 2 hrs. at 0° and 4 hrs. at ambient temperature, held 12 hrs. longer, decomposed with NH₄Cl solution, followed by isolation of the product gave 88% 3-p-tolyl-3-

ethylazetidin-2-one (XIV), m. 73-6° (petr. ether). XIV (15 g.) and 12 g. LiAlH₄ in absolute Et₂O, refluxed 5 hrs., cooled to 0°, and decomposed with the equivalent amount of 10% NH₄Cl solution gave 79% 3-p-tolyl-3-ethylazetidine (XV), b_{0.5} 89-91°; picrate m. 208-10° (EtOH); N-carbamoyl derivative m. 175-8° (EtOH-H₂O). XV (5 g.) treated with 15 cc. V gave 80% N-propionyl-3-p-tolyl-3-ethylazetidine, b_{0.5} 140-5°. N-Propionyl-3-phenyl-3-ethylazetidine (15 g.) added dropwise with stirring over a 2-hr. period to 50 cc. fuming HNO₃ at -35°, the temperature allowed to rise to 15° during 45 min., stirred an addnl. 30 min., poured onto 400 cc. crushed ice, neutralized at less than 10° with solid NaHCO₃, and the product isolated and distilled gave 81% N-propionyl-3-(p-nitrophenyl)-3-ethylazetidine (XVI), yellow oil, b_{0.3} 185-95°. XVI (5 g.) in 25 cc. 10% HCl, refluxed 30 min. with 25 cc. concentrated HCl, extracted with Et₂O, the aqueous phase alkalinized with 5% NaOH and further extracted with Et₂O, the residue from the second Et₂O extract taken up in absolute EtOH and treated with gaseous HCl gave 2.9 g. crude 3-(p-nitrophenyl)-3-ethylazetidine hydrochloride (XVII), m. 229-31° (absolute EtOH). XVI (5 g.) in 80 cc. absolute EtOH was reduced with H and 3 g. 10% Pd-C at 20° to give N-propionyl-3-(p-aminophenyl)-3-ethylazetidine, b_{0.3} 180-5°, which gave with Et₂O-HCl N-propionyl-3-(p-aminophenyl)-3-ethylazetidine hydrochloride (hygroscopic), m. 218-20°. XVII (7.8 g.) similarly hydrogenated and hydrolyzed yielded 1.1 g. 3-(p-aminophenyl)-3-ethylazetidine (XVIII), b_{0.4} 135-40°. XVIII gave from Et₂O solution with CO₂ the hygroscopic carbonate (XIX), m: 180-2° (decomposition). The structure of XVIII was confirmed by treating 5 g. 3-(p-aminophenyl)-3-ethylazetidin-2-one with 4 g. LiAlH₄ in absolute Et₂O, refluxing 6 hrs., decomposing with 20% NH₄Cl solution, extracting with Et₂O, and treating the Et₂O solution with CO₂ to obtain a precipitate of XIX, which on acidification and extraction gave XVIII.

IT Nervous system

(pharmaceuticals affecting central)

IT Carbonic acid, compound with 3-(p-aminophenyl)-3-ethylazetidine (1:2)

IT 503-29-7, Azetidine

(derivs.)

IT 2610-30-2, Azetidine, 3-ethyl-3-(p-nitrophenyl)-1-propionyl- 91429-46-8,

Azetidine, 3-(p-aminophenyl)-3-ethyl- 91562-32-2, Azetidine,

3-ethyl-3-p-tolyl- 91639-69-9, 2-Azetidinone, 3-ethyl-3-p-tolyl-

92250-45-8, Butyric acid, 2-cyano-2-p-tolyl-, ethyl ester 92322-85-5,

Hydratropic acid, β-amino-α-ethyl-p-methyl-, ethyl ester

92373-70-1, Azetidine, 3-(p-aminophenyl)-3-ethyl-1-propionyl-

92698-64-1, 2-Azetidinone, 3-[2-(diethylamino)ethyl]-3-phenyl-

92728-77-3, Azetidine, 3-ethyl-1-propionyl-3-p-tolyl- 92728-78-4,

Azetidine, 3-isopropyl-3-phenyl-1-propionyl- 93147-60-5, Azetidine,

3-butyl-3-phenyl-1-propionyl- 93151-26-9, Azetidine,

3-[2-(diethylamino)ethyl]-3-phenyl- **93428-62-7**,

1-Azetidinecarboxamide, 3-ethyl-3-p-tolyl- 93432-85-0, Azetidine,

3-ethyl-1-lactoyl-3-phenyl- 93540-55-7, Hydratropic acid,

β-amino-α-[2-(diethylamino)ethyl]-, ethyl ester 93999-28-1,

Azetidine, 1-(N,N-diethyl-β-alanyl)-3-ethyl-3-phenyl- 93999-29-2,

Azetidine, 3-[2-(diethylamino)ethyl]-3-phenyl-1-propionyl- 94069-34-8,

Azetidine, 3-ethyl-3-p-tolyl-, picrate 94759-27-0, Hydratropic acid,

β-amino-α-ethyl-p-methyl-, ethyl ester, picrate 94980-72-0,

Azetidine, 3-ethyl-3-(p-nitrophenyl)-, hydrochloride 96977-42-3, Butyric

acid, 2-cyano-4-(diethylamino)-2-phenyl-, ethyl ester 97379-95-8,

Azetidine, 3-(p-aminophenyl)-3-ethyl-1-propionyl-, hydrochloride

100175-47-1, Azetidine, 3-ethyl-1-(3-morpholinopropionyl)-3-phenyl-,

hydrochloride 101404-11-9, Azetidine, 1-(N,N-diethyl-β-alanyl)-3-

ethyl-3-phenyl-, citrate 101612-85-5, Azetidine, 3-(p-aminophenyl)-3-

ethyl-, carbonate

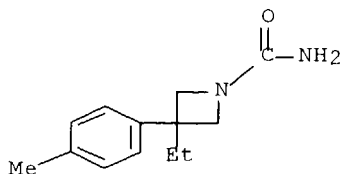
(preparation of)

IT **93428-62-7**, 1-Azetidinecarboxamide, 3-ethyl-3-p-tolyl-

(preparation of)

RN 93428-62-7 ZCAPLUS

CN 1-Azetidinecarboxamide, 3-ethyl-3-p-tolyl- (7CI) (CA INDEX NAME)



L37 ANSWER 7 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN

AN 1963:66370 ZCAPLUS Full-text

DN 58:66370

OREF 58:11311f-h,11312a-d

ED Entered STN: 22 Apr 2001

TI Substances acting on the central nervous system. XXVIII. On additional 3-substituted 2-azetidinones

AU Cignarella, Giorgio; Cristiani, Gian F.; Testa, Emilio

CS Lepetit S.p.A., Milan

SO Ann. (1963), 661, 181-7

DT Journal

LA Unavailable

CC 37 (Heterocyclic Compounds (One Hetero Atom))

OS CASREACT 58:66370

GI For diagram(s), see printed CA Issue.

AB cf. CA 56, 12875f. R'RNCH₂CETPhCO₂Et (I) (R = R' = H) (Ia) (CA 53, 6196c) (22 g.), 21 g. PrI, 21 cc. Et₃N, and 50 cc. absolute C₆H₆ refluxed 6 hrs., cooled, treated with 50 cc. H₂O, the organic layer separated, the aqueous layer extracted repeatedly with Et₂O, the combined organic solns. dried, and fractionated gave 20.5 g. I (R' = Pr, R = H) (II), b_{0.6} 110°. Ia (22 g.), 21 g. iso-PrI, 101 cc. Et₃N, and 150 cc. absolute C₆H₆ heated 8 hrs. at 130° in an N atmospheric in an autoclave, the contents cooled, filtered, and the filtrate fractionated gave 16 g. crude I (R' = iso-Pr, R = H), b_{0.15} 88°. Ia (22 g.), 16.5 g. BuBr, 20.6 cc. Et₃N, and 50 cc. absolute C₆H₆ refluxed 7 hrs., worked up as above, and redistd. gave 10.8 g. I (R = Bu, R' = H), b_{0.4} 114°. Ia (22 g.) in 20 cc. MeOH added to 11 g. BzH in 15 cc. MeOH, the whole heated 5 min. at 50° kept 12 hrs. at room temperature [concentration in vacuo of a sample gave I (RR' = benzylidene), nondistillable oil]; diluted to 150 cc. with MeOH, treated with 40 cc. H₂O, hydrogenated over 4 g. 10% Pd-C at room temperature and normal pressure (after 2 hrs. H absorption ceased), filtered, evaporated in vacuo, the residual oil dissolved in Et₂O, the solution dried, and treated with dry HCl gave 15 g. I (R = PhCH₂, R' = H) (III) HCl salt, m. 200-3°; pure III.HCl m. 203-6° (reconversion to base and then to III.HCl, then recrystn. from EtOH); from 15 g. III. HCl was isolated 12 g. crude III. EtMgBr solution (from 5.75 g. Mg in 40 cc. absolute Et₂O and 27.5 g. EtBr in 220 cc. absolute C₆H₆) treated dropwise during 30 min. with 19.5 g. II at 5°, the whole stirred 2 hrs. at 0° and 4 hrs. at room temperature, treated with 40 cc. cold 2N H₂SO₄ at 0° the organic layer separated, the aqueous layer repeatedly extracted with C₆H₆, the combined organic solns. washed neutral, dried, and fractionated gave 23% IV (R = Pr), b_{0.4} 115°. The following IV were similarly prepared (R, % yield, and b.p./mm. given): iso-Pr, 27, 104°/0.4; Bu, 60, 105-10°/0.5; PhCH₂, 74, 170°/0.6. Typical preps. Method A. 3-Methyl-3-phenyl-2-azetidinone (T., et al., loc. cit.) (8 g.) and 5.9 g. PhNCO in 80 cc. absolute PhMe refluxed 20 hrs., the

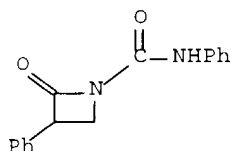
solution concentrated, the residue heated in vacuo (to 140°/1.5 mm.), and the residual product recrystd. from MeOH gave 40% V (R = R' = Ph, R' = Me), m. 84-5°. Method B. 3-Ethyl-3-phenyl-2-azetidinone (VI) (T., et al., loc. cit.) (10.5 g.) and 7.5 g. PhNCO heated 3 hrs. at 170°, the melt cooled, and crystallized from 40 cc. MeOH gave 62% V (R = R' = Ph, R' = Et), m. 89-91°. The following V were similarly prepared (R' = Ph in all cases) (R, R', method, % yield, m.p. given): Ph, H, A, 60, 86-8°; Ph, Et, A, 35, 95-7°; Ph, Pr, A, 23, -- (b1 155-60°); Ph, iso-Pr, A, 37, 127-9°; Ph, Bu, A, 18, 96-7°; Et, Et, A, 79, -- (b1.5 165-70°); Ph, Ph, B, 87, 160-1°. VI (10.5 g.) and 5.94 g. BuNCO in 150 cc. absolute PhMe refluxed 40 hrs. and fractionated gave a forerun, b0.4 110-30°, chiefly VI, and 1.25 g. V (R = Ph, R' = Et, R' = Bu), b0.4 165-70° v 1740, 1700, and 1530 cm.-1 VI (3.5 g.) and 2 cc. 38% aqueous HCHO in 35 cc. EtOH heated to boiling, treated dropwise with 1.65 g. pyrrolidine in 5 cc. EtOH, boiled 30 min., evaporated in vacuo, the residual oil dissolved in Et2O, the solution extracted with 10% HCl, the extract made alkaline with 10% aqueous NaOH, and the product isolated with Et2O gave 85% VII (R = Ph, R' = Et, R'' = pyrrolidino), b0.2 140°. The following VII were similarly prepared (R, R', R'', % yield, b.p./mm. given): Ph, H, pyrrolidino, 72, 145-50°/4; p-MeOC6H4, H, pyrrolidino, 88, 170-5°/0.2 (m. 50.5-1.0°); Et, Et, pyrrolidino, 86, 95-100°/0.4; Et, Et, Me2N, 125°/0.4; Ph, Et, morpholino, 86, 94-5° (Et2O); Ph, Et, 3,3-dimethylazetidin, 72, 135-40°/0.4; Ph, iso-Pr, pyrrolidino, 77, 140°/0.4; Ph, Bu, pyrrolidino, 45, 140°/0.5; Ph, PhCH2, pyrrolidino, 77, -- [m. 130-3° (EtOH)].

- IT Nervous system
(pharmaceuticals affecting central)
- IT 930-21-2, 2-Azetidinone
(derivs.)
- IT 1886-39-1, 2-Azetidinone, 3-ethyl-1-isopropyl-3-phenyl- 91346-42-8,
2-Azetidinone, 1-[(dimethylamino)methyl]-3,3-diethyl-(?) 91695-53-3,
2-Azetidinone, 3,3-diethyl-1-(1-pyrrolidinylmethyl)- 92292-11-0,
2-Azetidinone, 3-phenyl-1-(1-pyrrolidinylmethyl)- 92292-62-1,
1-Azetidinecarboxanilide, 3,3-diethyl-2-oxo- 92499-42-8, 2-Azetidinone,
3-ethyl-3-phenyl-1-propyl- 92728-79-5, 2-Azetidinone,
1-butyl-3-ethyl-3-phenyl- **93013-67-3**, 1-Azetidinecarboxanilide,
2-oxo-3-phenyl- 93145-60-9, Butyric acid, 2-[(isopropylamino)methyl]-2-
phenyl-, ethyl ester 93145-61-0, Butyric acid, 2-phenyl-2-
[(propylamino)methyl]-, ethyl ester **93331-24-9**,
1-Azetidinecarboxanilide, 3-methyl-2-oxo-3-phenyl- 93735-81-0, Butyric
acid, 2-[(butylamino)methyl]-2-phenyl-, ethyl ester **93879-35-7**,
1-Azetidinecarboxanilide, 3-ethyl-2-oxo-3-phenyl- 93990-06-8,
2-Azetidinone, 3-butyl-3-phenyl-1-(1-pyrrolidinylmethyl)- 94064-33-2,
2-Azetidinone, 3-(p-methoxyphenyl)-1-(1-pyrrolidinylmethyl)- 94373-35-0,
2-Azetidinone, 1-[(diethylamino)methyl]-3-ethyl-3-phenyl-(?) 94576-32-6,
Butyric acid, 2-[(benzylideneamino)methyl]-2-phenyl-, ethyl ester
94911-61-2, Butyric acid, 2-[(benzylamino)methyl]-2-phenyl-, ethyl ester,
hydrochloride 94911-62-3, Butyric acid, 2-[(benzylamino)methyl]-2-phenyl-
, ethyl ester 94916-58-2, 2-Azetidinone, 3-benzyl-3-phenyl-1-(1-
pyrrolidinylmethyl)- **95163-69-2**, 1-Azetidinecarboxanilide,
2-oxo-3,3-diphenyl- 95427-20-6, 2-Azetidinone, 1-benzyl-3-ethyl-3-phenyl-
96972-99-5, 1-Azetidinecarboxanilide, 3-butyl-2-oxo-3-phenyl-
96977-11-6, 2-Azetidinone, 1-[(3,3-dimethyl-1-azetidiny)methyl]-3-ethyl-3-
phenyl- 96977-12-7, 2-Azetidinone, 3-isopropyl-3-phenyl-1-(1-
pyrrolidinylmethyl)- **97020-54-7**, 1-Azetidinecarboxamide,
N-butyl-3-ethyl-2-oxo-3-phenyl- 97020-56-9, 2-Azetidinone,
3-ethyl-1-(morpholinomethyl)-3-phenyl- **97077-29-7**,
1-Azetidinecarboxanilide, 3-isopropyl-2-oxo-3-phenyl- **97077-30-0**
, 1-Azetidinecarboxanilide, 2-oxo-3-phenyl-3-propyl- 98132-64-0,
2-Azetidinone, 3-ethyl-3-phenyl-1-(1-pyrrolidinylmethyl)-
(preparation of)
- IT **93013-67-3**, 1-Azetidinecarboxanilide, 2-oxo-3-phenyl-

(preparation of)

RN 93013-67-3 ZCAPLUS

CN 1-Azetidinecarboxanilide, 2-oxo-3-phenyl- (7CI) (CA INDEX NAME)



L37 ANSWER 8 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN

AN 1962:45914 ZCAPLUS Full-text

DN 56:45914

OREF 56:8660i,8661a-i,8662a

ED Entered STN: 22 Apr 2001

TI Substances acting on the central nervous system. XIV. 3,3-Disubstituted azetidines

AU Testa, I. Emilio; Fontanella, Luigi; Mariani, Luigi; Cristiani, Gian Franco

CS Lepetit S.p.A., Milan

SO Ann. (1960), 633, 56-66

DT Journal

LA Unavailable

CC 31 (Heterocyclic Compounds-One Hetero Atom)

AB cf. CA 53, 17958f; 54, 3361h; 54, 3362d; 55, 27270f. I were prepd. and reduced with LiAlH_4 to II. Some N-methylazetidines were prepared from azetidines and MeI or $\text{HCO}_2\text{HCH}_2\text{O}$. The NaCNO -3,3-dialkylazetidine reaction gave I ($\text{R}_2 = \text{NH}_2$) (III). A mixture of 3.22 g. 3-ethyl-3-phenylazetidine and 0.8 g. AcCl was kept at ice- NaCl temperature for 30 min., then at room temperature 1 hr.; decomposition with 10 ml. ice water, extraction with Et_2O , and distillation of the washed and dried (Na_2SO_4) extract gave 1 g. I ($\text{R} = \text{Et}$, $\text{R}_1 = \text{Ph}$, $\text{R}_2 = \text{Me}$), b0.4 155-65°. The following I were similarly prepared (R , R_1 , R_2 , and b.p. given): Et, Ph, Et, b0.6 130-50°; Et, Ph, Pr, b0.2 140°; Et, Ph, Bu, b0.5 150°; Et, Ph, iso-Bu, b0.2 145-50°; Et, Ph, Me_3C , b0.4 140° [m. 72-4° (ligroine)]; Et, Ph, CH_2Ph , b0.5 190-5°; Et, $(\text{CH}_2)_2\text{Ph}$, b0.3 180-90°; Et, Ph, Ph, -- [m. 63-4° (ligroine)]; Et, Ph, OEt, b1 125-30°; Me, Me, OEt, b24 100-2°. A mixture of 4.6 g. 3,3-dipropylazetidine and 14 ml. Ac_2O was kept at 110-115° for 1 hr., poured into 35 ml. 60° water, brought to pH 6 with Na_2CO_3 solution, and extracted with Et_2O . The extract was washed (Na_2CO_3 solution, water), dried (Na_2SO_4), and distilled to give 4.17 g. I ($\text{R} = \text{R}_1 = \text{Pr}$, $\text{R}_2 = \text{Me}$), b0.4 96-100°. Similarly the following were prepared (R , R_1 , R_2 , and b.p. given): Me, Ph, Et, b0.4 150-60°; Me, Ph, Me, b0.4 135-40°; Ph, Pr, Et, b0.2 135-45°; Bu, Ph, Me, b0.2 155-65°; Ph, CH_2Ph , Me, -- [m. 115-17° (EtOH)]; Ph, CH_2Ph , Et, -- [m. 79-80° (aqueous EtOH)]; Me, Me, Me, b15 80-90°; Et, Et, Me, b0.4 85-90°; Et, Et, Et, b0.2 85-9°; Bu, Bu, Me, b0.4 108-10°. The following III were prepared by the acyl halide- Et_3N method (R , R_1 , b.p., and m.p. given): Et, Ph, --, 149-50°; Me, Me, b0.4 180-6°, 57-61°; Et, Et, b0.2 200-10°, 40-5°. A suspension of 1.5 g. LiAlH_4 in 30 ml. absolute Et_2O was added dropwise to a solution of 3 g. I in 20 ml. Et_2O , the mixture was refluxed 3 hrs., treated with 10% NH_4Cl at 0°, filtered, and the filtrate extracted with Et_2O . The dry (Na_2SO_4) extract was distilled to give 2.05 g. II ($\text{R} = \text{Et}$, $\text{R}_1 = \text{Ph}$, $\text{R}_2 = \text{Me}$) (V), b0.6-0.8 75-80°. Similarly the following II were prepared (R , R_1 , R_2 , and b.p. given): Et, Ph, H, b0.4 85-90°; Et, Ph, Pr, b0.2 90°; Et, Ph, Bu, b0.4 98-100°; Et, Ph, iso-Bu, b0.2 95°; Et, Ph, Me_3C , b0.3 88-90°; Et, Ph, CH_2Ph , b0.2 130°; Et, Ph, $(\text{CH}_2)_2\text{Ph}$, b0.4 150°; Pr, Pr, Me, b21 105-10°; Bu, Bu, Me, b10 103-5°. By the same method the following IV were prepared (R ,

R1, and b.p. given): Et, Ph (VI), --[m. 62-4° (EtOH)]; Me, Me (VII), b0.6 100-5°; Et, Et (VIII), b0.2-0.4 135-45°. A suspension of 3 g. LiAlH₄ in 30 ml. absolute Et₂O was added dropwise to a mixture of 10 g. 3-ethyl-3-phenylazetidine, 6.3 g. AcOEt, and 50 ml. absolute Et₂O, refluxed 150 min., cooled to 0°, and decomposed with 5 ml. 10% NH₄Cl. The suspension was filtered, the filtrate and the residue were extracted with Et₂O and the dried (Na₂SO₄) extract was distilled to give 9 g. II (R = Et, R1 = Ph, R2 = Me), b0.7 75-80°. Similarly the following II were prepared (R, R1, R2, and b.p. given): Et, Ph, Et, b0.4 90-5°; Et, Ph, Ph, b0.4 138-40°; Me, Ph, Me, b0.6 62-5°; Ph, Pr, Me, b0.2 80-2°; Ph, iso-Pr, Me, b0.5-0.6 80-2°; Bu, Ph, Me, b0.6 83-5°; Ph, CH₂Ph, Me, b0.5-0.6 130-4°; Ph, cyclohexyl, Me, b0.2-0.3 120-3°; Me, Ph, CH:CHPh, b0.4 130-3°. 3,3-Dimethylazetidine-2H₂O (2 g.) treated with 2 ml. MeI in 50 ml. absolute Et₂O gave 3.26 g. 1,3,3-trimethylazetidine-HI, m. 138-40°. Similarly, 1,3-dimethyl-3-phenylazetidine-HI, m. 132-5° (decomposition), was obtained from 3-methyl-3-phenylazetidine, 1-methyl-3-ethyl-3-phenylazetidine-HI, m. 131-5° (decomposition), from 3-ethyl-3-phenylazetidine. V treated with MeI gave V.MeI, m. 130° (decomposition). Similarly, VI gave a dimethiodide, m. 100° (decomposition), VII gave a dimethiodide, m. 126-8°, and VIII gave a dimethiodide, m. 180-1° (decomposition). II (R = Et, R1 = Ph, R2 = H) was also prepared from 5 g. 3-ethyl-3-phenylazetidine, 46.5ml. HCO₂H, and 3.25 ml. 27.8% CH₂O. The mixture was heated to 105-10° for 150 min., partially evaporated in vacuo, diluted with water, neutralized with Na₂CO₃, and extracted with Et₂O. The extract was distilled and 2.39 g. product [picrate m. 118-20° (EtOH)] was obtained. A solution of 5 g. 3-ethyl-3-phenylazetidine in 30 ml. HCO₂H heated to 120-30° for 1 hr gave upon distillation 4.4 g. 3-ethyl-3-phenyl-1-formylazetidine, b0.6 125-8°, m. 62-4°. 3-Ethyl-3-phenylazetidine (3.2 g.) in 20 ml. N HCl treated with 1.3 g. NaOCN for 15 min. at 50-60° gave 3.6 g. III (R = Et, R1 = Ph), m. 154-6° (5% EtOH). Similarly the following III were prepared from the corresponding 3,3-dialkylazetidines [R, R1 and m.p. (aqueous EtOH unless specified) given]: Me, Ph, 176°; Ph, Pr, 165-6°; Ph, iso-Pr, 158-60°; Bu, Ph, 129-31°; Ph, CH₂Ph, 159-61°; Ph, cyclohexyl, 172-4°; Me, Me, 182-4° (water); Et, Et, 179-80°; Bu, Bu, 114-15°.

- IT Azetidine, 1-acetyl-3-ethyl-3-phenyl-
 Azetidinium compounds, 1,1'-hexamethylenebis-, [1,3,3-trimethyl-iodide]
 Azetidinium compounds, 1,1'-hexamethylenebis-, [3,3-diethyl-1-methyl-iodide]
 Azetidinium compounds, 1,1'-hexamethylenebis-, [3-ethyl-1-methyl-3-phenyl-iodide]
 Azetidinium compounds, 1,3-diethyl-1-methyl-3-phenyl-, iodide
 IT 503-29-7, Azetidine
 (derivs.)
 IT 7215-26-1, Azetidine, 1-ethyl-3-methyl-3-phenyl- 14384-18-0, Azetidine, 1-acetyl-3,3-dimethyl- 88590-75-4, Azetidine, 1,1'-hexamethylenebis[3,3-dimethyl- 88782-88-1, Azetidine, 1-benzyl-3-ethyl-3-phenyl- 88782-89-2, Azetidine, 3-benzyl-1-ethyl-3-phenyl- 90152-13-9, 1-Azetidinecarboxamide, 3,3-diethyl- 90204-71-0, 1-Azetidinecarboxylic acid, 3,3-dimethyl-, ethyl ester 90485-46-4, 1-Azetidinecarboxamide, 3,3-dimethyl- 91016-01-2, Azetidine, 3,3-diethyl-1-propionyl- 91055-59-3, Azetidine, 1-acetyl-3,3-diethyl- **91180-59-5**, 1-Azetidinecarboxamide, 3-methyl-3-phenyl- 91248-93-0, Azetidine, 1-ethyl-3,3-dipropyl- 91369-91-4, Azetidine, 1-acetyl-3,3-dipropyl- **91556-81-9**, 1-Azetidinecarboxamide, 3-ethyl-3-phenyl- 91562-31-1, Azetidine, 3-ethyl-1-methyl-3-phenyl- 91564-98-6, 1-Azetidinecarboxamide, 3,3-dibutyl- 91639-65-5, Azetidine, 1-acetyl-3-methyl-3-phenyl- 91725-13-2, Azetidine, 1,3,3-trimethyl-, hydriodide 92030-72-3, Azetidine, 1-acetyl-3,3-dibutyl- 92039-67-3, Azetidine, 3-methyl-3-phenyl-1-propionyl- 92162-13-5, Azetidine, 3,3-dibutyl-1-ethyl- 92195-22-7, Azetidine, 1,3-diethyl-3-phenyl- 92320-90-6, Azetidine, 1-ethyl-3-isopropyl-3-phenyl- 92320-91-7,

Azetidine, 1-ethyl-3-phenyl-3-propyl- **92373-71-2**,
 1-Azetidinecarboxamide, 3-butyl-3-phenyl- 92499-41-7, Azetidine,
 3-ethyl-3-phenyl-1-propionyl- 92500-19-1, 1-Azetidinecarboxylic acid,
 3-ethyl-3-phenyl-, ethyl ester 92725-13-8, Azetidine,
 1-butyl-3-ethyl-3-phenyl- 92725-14-9, Azetidine, 3-butyl-1-ethyl-3-
 phenyl- 92728-75-1, Azetidine, 1-acetyl-3-butyl-3-phenyl- 92728-76-2,
 Azetidine, 1-butyryl-3-ethyl-3-phenyl- 93085-83-7, 1-
 Azetidinecarboxaldehyde, 3-ethyl-3-phenyl- 93143-91-0, Azetidine,
 1,1'-adipoylbis[3,3-dimethyl- 93144-82-2, Azetidine,
 3-ethyl-1-isopentyl-3-phenyl- 93144-83-3, Azetidine,
 3-ethyl-1-pentyl-3-phenyl- 93147-61-6, Azetidine, 3-ethyl-1-isovaleryl-3-
 phenyl- 93147-62-7, Azetidine, 3-ethyl-3-phenyl-1-pivaloyl-
 93147-63-8, Azetidine, 3-ethyl-3-phenyl-1-valeryl- **93428-63-8**,
 1-Azetidinecarboxamide, 3-isopropyl-3-phenyl- **93428-64-9**,
 1-Azetidinecarboxamide, 3-phenyl-3-propyl- **93648-59-0**,
 1-Azetidinecarboxamide, 3-benzyl-3-phenyl- 93720-28-6, Azetidine,
 3-ethyl-3-phenyl-1-propyl- 93810-62-9, Azetidine, 3-cyclohexyl-1-ethyl-3-
 phenyl- 94069-33-7, Azetidine, 3-ethyl-1-methyl-3-phenyl-, picrate
 94164-05-3, Azetidine, 1-acetyl-3-benzyl-3-phenyl- 94164-06-4,
 Azetidine, 1-benzoyl-3-ethyl-3-phenyl- 94310-34-6, Azetidine,
 1-cinnamyl-3-methyl-3-phenyl- 94327-11-4, Azetidine,
 3-phenyl-1-propionyl-3-propyl- 94384-30-2, Azetidine,
 1,3-diethyl-3-phenyl-, picrate 94521-84-3, Azetidine,
 1,3-dimethyl-3-phenyl-, hydriodide 94575-87-8, Azetidine,
 3-ethyl-1-hydrocinnamoyl-3-phenyl- 94676-39-8, Azetidine,
 1,1'-adipoylbis[3,3-diethyl- 94677-05-1, Azetidine, 1,1'-
 hexamethylenebis[3,3-diethyl- 94910-73-3, Azetidine,
 3-ethyl-3-phenyl-1-(3-phenylpropyl)- 94913-33-4, Azetidine,
 3-ethyl-1-phenethyl-3-phenyl- 95317-33-2, Azetidine,
 3-benzyl-3-phenyl-1-propionyl- 95317-34-3, Azetidine,
 3-ethyl-3-phenyl-1-(phenylacetyl)- 95467-30-4, Azetidine,
 3-ethyl-1-methyl-3-phenyl-, hydriodide 96273-28-8, Azetidine,
 1,1'-adipoylbis[3-ethyl-3-phenyl- 96274-71-4, Azetidine,
 1,1'-hexamethylenebis[3-ethyl-3-phenyl- **97020-08-1**,
 1-Azetidinecarboxamide, 3-cyclohexyl-3-phenyl- 97739-23-6, Azetidine,
 3-ethyl-1-neopentyl-3-phenyl-

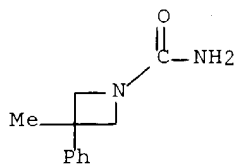
(preparation of)

IT **91180-59-5**, 1-Azetidinecarboxamide, 3-methyl-3-phenyl-

(preparation of)

RN 91180-59-5 ZCAPLUS

CN 1-Azetidinecarboxamide, 3-methyl-3-phenyl- (7CI) (CA INDEX NAME)



L37 ANSWER 9 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN

AN 1962:2337 ZCAPLUS Full-text

DN 56:2337

OREF 56:453c-e

ED Entered STN: 22 Apr 2001

TI 1-Carbamoyl-3-substituted azetidines

IN Testa, Emilio; Fontanella, Luigi; Maffii, Giulio
 PA Lepetit S.p.A.
 SO Division of Brit. 872,446
 DT Patent
 LA Unavailable

CC 31 (Heterocyclic Compounds-One Hetero Atom)

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 872447		19610712	GB	<--
DE 1147585			DE	
FR 1332510			FR	
US 3094518		1963	US	<--

PI GB 872447 19610712 GB <--
 DE 1147585 DE
 FR 1332510 FR
 US 3094518 1963 US <--

AB (preceding abstr.). The title compds. were prepd. by reaction of a 3-substituted azetidine (Brit. 872,446) with an equimolar amount of an alkali metal cyanate in H₂O at 50-100°. Thus, 32 g. 3-phenyl-3-ethylazetidine in 100 ml. H₂O was treated with 100 ml. 2N HCl then 13 g. NaOCN, the mixture heated 15 min. at 50-60°, and cooled to yield 88% 1-carbamoyl-3-phenyl-3-ethylazetidine, m. 154-6° (5% EtOH). The following 1-carbamoylazetidines were prepared (3,3-substituents, % yield, and m.p. given): Ph, Me (I), 90, 176°; Ph, H, 80, 231-3°; Et, Et, 77, 179-80°; Ph, Pr, 87, 165-6°; Ph, benzyl, 81, 159-61°; Bu, Bu, 90, 114-15°; Ph, Bu, 75, 129-31° Ph, iso-Pr (II), 86, 158-60° Ph, cyclohexyl, 62, 172-4°; and Ph, Me, 64.5, 176°. These compds. were active as sedatives, hypnotics, and antispasmodic agents; the last effect was particularly high with 1-carbamoyl-3-propylazetidine, I, and II, which in doses <20 mg./kg. prevented convulsive seizures induced by pentamethylenetetrazole. The average lethal dosage, L.D.50. was very high, in all cases exceeding 300-400 mg./kg. on intraperitoneal administration to rats.

IT Sedatives

(1-azetidinecarboxamides)

IT Antispasmodics

Hypnotics

(1-azetidinecarboxamides as)

IT 503-29-7, Azetidine 5661-52-9, 1-Azetidinecarboxamide
 (derivs.)

IT 90152-13-9, 1-Azetidinecarboxamide, 3,3-diethyl- 90917-68-3,
 1-Azetidinecarboxamide, 3-phenyl- 91180-59-5,
 1-Azetidinecarboxamide, 3-methyl-3-phenyl- 91556-81-9,
 1-Azetidinecarboxamide, 3-ethyl-3-phenyl- 91564-98-6,
 1-Azetidinecarboxamide, 3,3-dibutyl- 92373-71-2,
 1-Azetidinecarboxamide, 3-butyl-3-phenyl- 93428-63-8,
 1-Azetidinecarboxamide, 3-isopropyl-3-phenyl- 93428-64-9,
 1-Azetidinecarboxamide, 3-phenyl-3-propyl- 93648-59-0,
 1-Azetidinecarboxamide, 3-benzyl-3-phenyl- 97020-08-1,
 1-Azetidinecarboxamide, 3-cyclohexyl-3-phenyl-

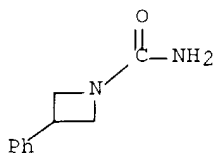
(preparation of)

IT 90917-68-3, 1-Azetidinecarboxamide, 3-phenyl-

(preparation of)

RN 90917-68-3 ZCAPLUS

CN 1-Azetidinecarboxamide, 3-phenyl- (6CI, 7CI) (CA INDEX NAME)



L37 ANSWER 10 OF 10 ZCAPLUS COPYRIGHT 2004 ACS on STN

AN 1961:124751 ZCAPLUS Full-text

DN 55:124751

OREF 55:23481e-i,23482a-c

ED Entered STN: 22 Apr 2001

TI Substances acting on the central nervous system. XVIII. 3-Phenylazetidine

AU Testa, Emilio; Fontanella, Luigi; Mariani, Luigi; Cristiani, Gianfranco

CS Lepetit S.p.A., Milan

SO Ann. (1961), 639, 157-65

DT Journal

LA Unavailable

CC 10G (Organic Chemistry: Heterocyclic Compounds)

OS CASREACT 55:124751

AB cf. CA 55, 7529i. Hydrogenating NCCHPhCO₂Et in abs. EtOH and HCl in the presence of 5% Pd-C 30 min. at room temperature/1 atmospheric gave Et α -phenyl- β -aminopropionate-HCl (I.HCl), m. 164-5°. I (90 g.) and the Grignard compound from 38.6 g. Mg and 250 g. MeI in 800 ml. Et₂O 4 hrs. at 25° gave 51.5% 3-phenyl-2-azetidinone (II), m. 114-16°. II with LiAlH₄ in Et₂O gave 3-phenylazetidine (III), b_{3.5} 87-9°; picrate m. 149-50°; hydrochloride m. 78-80°; H sulfate m. 110-12°. Treating III with (A) acid chlorides in the presence of Et₃N or (B) acid anhydrides yielded N-acyl derivs. The following PhCH₂.CH₂.NR.CH₂ (IV) (R = acyl) were thus prepared (R, method, % yield, and b.p./mm. or m.p. given): Ac, B, 88, 135-7°/1; COEt, B, 54, 125°/0.6; CPh, B, 75, 131-3°/0.4; CO₂Et, A, 50, 105-7°/0.3; 3,4,5-(MeO)3C₆H₂CO, A, 69, 109-11°; CONEt₂, A, 78, 130-3°/0.6; SO₃H, A, 60, 185-7° (decomposition); p-MeC₆H₄SO₂, A, 48, 133-6°. IV (R = alkyl), were obtained by (A) reducing IV (R = acyl) with LiAlH₄ in Et₂O, (B) boiling III in benzene with R halides in presence of Et₃N, or (C) boiling 5 g. III and 7.7 g. Et cinnamate with 2.2 g. LiAlH₄ in Et₂O 2.5 hrs., pouring into 20% NH₄Cl, extracting with Et₂O, shaking the Et₂O layer with 10% HCl, neutralizing the acid layer then with 10% NaOH, and extracting with Et₂O. The Et₂O extract worked up gave 30% IV (R = cinnamyl), b_{0.6} 155-60°. Quaternary methiodides were obtained by treating IV (R = alkyl) in Et₂O with MeI. The following IV (R = alkyl) and the corresponding MeI salts were thus prepared [R, method, % yield, b.p./mm. of IV (R = alkyl), and decomposition point of the corresponding MeI salt given]: Me, A, 87, 62-4°/2, 137-9°; Et, A(C), 77(56), 110-15°/8, 114-16°; CH₂Ph, B(C), 64(33), 122-7°/0.4, 140-2°; iso-Pr, B, 35, 72-4°/0.8, 148-50°; Bu, A, 93, 83-5°/0.5, 121-3°; iso-Bu, B, 29, 74-5°/0.4, 110-12°; CH₂CH:CH₂, B, 51, 65°/0.3, 115-18°; CH₂CO₂Et, B, 29, 123-4°/0.5, 111-13°; 2,6-Me₂C₆H₃NHCOCH₂, B, 53, m. 113-16°, -. III (2 g.) in 40 ml. Et₂O treated with 2 ml. MeI yielded 1-methyl-3-phenylazetidine-HI, m. 107-10°. Boiling 1.75 g. III 15 min. with 0.85 g. NaOCN and 13.5 ml. N HCl gave 1.6 g. IV (R = carbamoyl), m. 231-3° (decomposition). Dropwise addition of 4.45 g. PhNCO to a benzene solution of 5 g. III gave IV (R = phenylcarbamoyl), m. 202-4°. Leaving 10 g. III and 3.6 g. ethylene oxide in absolute EtOH 86 hrs. at room temperature yielded IV (R = β -hydroxyethyl), b_{0.8} 110-15°, which in CHCl₃ treated with SOCl₂ 60 min. at 40-5°, cooled, poured into H₂O, and the CHCl₃ solution worked up gave IV (R = β -chloroethyl), b_{0.3} 90-3°; hydrochloride m. 136-8°. Adding 6 g. NaNO₂ portionwise to a cooled (-5°) solution of 2.5 g. III in 30 ml. 80% AcOH, raising the temperature slowly to 90°, and keeping at this temperature 1 hr. gave 2.1g. IV(R = NO), m. 33-5°. To 3.45g. LiAlH₄ in 120 ml. tetrahydrofuran was added dropwise 10 g. IV (R = NO) m 130 ml. tetrahydrofuran, the mixture stirred 2.25 hrs. at 40-5°, and worked up to give IV (R = NH₂), b_{0.5} 75-85°; hemimaleate m. 112-14°. Refluxing IV (R = NH₂.HCl) in H₂O with p-O₂NC₆H₄CHO in EtOH gave IV (R = p nitrobenzylideneamino), m. 112-14°.

IT Nervous system

(comps. affecting)

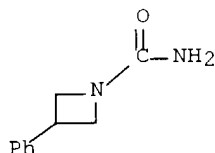
IT Azetidine, 1-(2-chloroethyl)-3-phenyl-, hydrochloride

Azetidine, 1-methyl-3-phenyl-, hydriodide

Azetidinium compounds, 1,1-dimethyl-3-phenyl-, iodide
 Azetidinium compounds, 1-(carboxymethyl)-1-methyl-3-phenyl-, iodide, Et ester

Azetidinium compounds, 1-allyl-1-methyl-3-phenyl-, iodide
 Azetidinium compounds, 1-benzyl-1-methyl-3-phenyl-, iodide
 Azetidinium compounds, 1-butyl-1-methyl-3-phenyl-, iodide
 Azetidinium compounds, 1-ethyl-1-methyl-3-phenyl-, iodide
 Azetidinium compounds, 1-isobutyl-1-methyl-3-phenyl-, iodide
 Azetidinium compounds, 1-isopropyl-1-methyl-3-phenyl-, iodide
 Maleic acid, compound with 1-amino-3-phenylazetidine

IT 4363-13-7, Azetidine, 3-phenyl-
 (and derivs.)
 IT 4363-16-0, Azetidine, 1-ethyl-3-phenyl- 7215-09-0, Azetidine,
 1-methyl-3-phenyl- 7215-11-4, 1-Azetidineethanol, 3-phenyl- 7215-12-5,
 Azetidine, 1-(2-chloroethyl)-3-phenyl- 7215-13-6, Azetidine,
 1-isopropyl-3-phenyl- 7215-14-7, Azetidine, 1-butyl-3-phenyl-
 7215-15-8, Azetidine, 1-isobutyl-3-phenyl- 7215-16-9, Azetidine,
 1-benzyl-3-phenyl- 7215-17-0, Azetidine, 1-allyl-3-phenyl- 7215-18-1,
 Azetidine, 1-cinnamyl-3-phenyl- 17197-57-8, 2-Azetidinone, 3-phenyl-
 29753-99-9, Hydratropic acid, β -amino-, ethyl ester, hydrochloride
 70892-07-8, Azetidine, 3-phenyl-1-p-tolylsulfonyl- **90917-68-3**,
 1-Azetidinecarboxamide, 3-phenyl- 91132-00-2, Azetidine,
 1-acetyl-3-phenyl- 91639-68-8, Azetidine, 3-phenyl-1-propionyl-
 98952-75-1, Azetidine, 1-nitroso-3-phenyl- 98996-49-7,
 1-Azetidinesulfonic acid, 3-phenyl- 99362-02-4, Azetidine,
 1-amino-3-phenyl- 100390-14-5, 1-Azetidinecarboxylic acid, 3-phenyl-,
 ethyl ester 100608-89-7, 1-Azetidineacetic acid, 3-phenyl-, ethyl ester
 100875-32-9, 1-Azetidinecarboxamide, N,N-diethyl-3-phenyl-
101279-71-4, 1-Azetidinecarboxanilide, 3-phenyl- 101283-07-2,
 Azetidine, 1-benzoyl-3-phenyl- 101284-96-2, Azetidine,
 1-(p-nitrobenzylideneamino)-3-phenyl- 102178-22-3, Azetidine,
 3-phenyl-1-(3,4,5-trimethoxy-benzoyl)- 112273-17-3, 1-Azetidineaceto-
 2',6'-xylidide, 3-phenyl- 115051-80-4, Azetidine, 1-amino-3-phenyl-,
 maleate
 (preparation of)
 IT **90917-68-3**, 1-Azetidinecarboxamide, 3-phenyl-
 (preparation of)
 RN 90917-68-3 ZCAPLUS
 CN 1-Azetidinecarboxamide, 3-phenyl- (6CI, 7CI) (CA INDEX NAME)



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